REGULATION OF GLUTAMATE UPTAKE IN EXPERIMENTAL EPILEPSY

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Glutamate (**GLU**) reuptake is the primary mechanism for its removal from the synapse. Several GLU transporters have been cloned, although their cellular localization and pharmacological profiles remain to be clearly established. We had previously identified at least two uptake systems in whole mouse brain synaptosomes (Cordero et al., 1994). In genetic audiogenic seizures (**AGS**), the uptake is elevated prior to the appearance of seizures. In contrast, mice with induced epilepsy (**AGS**) have decreased GLU uptake. This decrease can be largely prevented by treatment with MK-801. The effect of MK-801 on GLU uptake implies that postsynaptic events (NMDA blockade) regulates presynaptic process(es) (GLU uptake). Thus, we examined whether NO had any effect on GLU uptake. Synaptosomes preincubated with nitroarginine or aminoguanidine, NO synthase inhibitors, increase GLU uptake. Correspondingly, sodium nitroprusside, an NO donor, inhibited GLU uptake. In genetic AGS, however, these effects are not observed. Li^+, at millimolar concentrations potentiates GLU uptake, possibly by inhibiting phophatidylinositol turnover. In contrast, Li^+ has no effect on the uptake of GLU by synaptosomes from epileptic mice. Pertussis toxin, a protein G inhibitor causes a reduction in GLU uptake. Our results point to the regulation of GLU uptake by second messengers and its alteration in experimental epilepsy. (Supported by the NIH/MBRS, RCMI and CIDIC Institutional Programs and Animal Resource Center).

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